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COMMUNICATION: FROM MOLECULES TO MARS

Melvin Calvin

August 1962

COMMUNICATION: FROM MOLECULES TO MARS*

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Abstract

August 23, 1962

An analysis is made of the energetic, molecular, macromolecular and organizational steps which appear to be essential for the development of a living cell from a nonliving origin. Accepting the current view of the primitive atmosphere of the earth, experimental demonstration for the formation of the fundamental molecules of living organisms (amino acids, fatty acids, purines and pyrimidines) under the influence of available energy sources (ultraviolet light, ionizing radiation and electric discharge) is presented.

The combination of these small units and the polymers via the universal dehydration condensation reaction under the influence of pyrophosphate or carbon-to-nitrogen multiple bonds is experimentally provided. These macromolecules are shown to assume specific configurations resulting from intrinsic factors in their structure, and mechanisms for information transfer and energy transfer by virtue of these ordered structures are described. The aggregation of bifunctional molecules at interfaces to give ordered membranous structures is indicated as the possible source for the cell wall enclosures, thus completing the prebiotic phase.

Since this sequence of events on a molecular level may be expected to occur whenever and wherever the initial conditions arise, we are led to expect the appearance of life of this type elsewhere in the universe. Some of the evidence that is presently at hand regarding such extraterrestrial life is presented, and the promise of more definitive information, at least about the solar system, seems to be forthcoming.

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COMMUNICATION: FROM MOLECULES TO MARS

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INTRODUCTION

Ever since man became conscious of himself it seems he has been concerned with wonder at his own nature. In fact, the degree to which he has left evidence of this concern is frequently taken as a measure of his progress toward humanhood. Very early in his speculations about his own nature, he recognized that he was a member of a large class of objects on the surface of the earth which were called "living" as distinguished from those which were not.

Very soon, as a corollary or extension of his concern for this own nature, he therefore became interested in the nature of life and living things themselves. In the course of his history, both ancient and modern, he produced an enormous variety of notions about both the nature of life and his relation to it. But it has only been in the last century since the dominant success of Darwinian thought that man has been in a position to begin to devise patterns of thought within the framework of what we

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call rational science today. In fact, it has only been in the last two or three decades that both the biochemical and biophysical, as well as chemical and physical and astronomical, knowledge has reached the level that has enabled him to escape the requirement for use of such terms as "fields", "gradients", and "essences" and replace them with the more severely and accurately defined terms of chemical reaction, transformations, molecules and their interactions, crystals, and molecular films, about whose nature we need not guess.

This expanded particular knowledge about the atomic and molecular constituents of which living things are constructed, together with an increased understanding of the way in which these molecules (used in the most general sense) interact with each other, that is, communicate with each other so as to cooperate in the production of what we now recognize at least as living organisms, has had two very interesting results, among others. The first of these has been to stimulate scientists to create hypothetical schemes leading from the primeval nonliving earth to the present day¹⁻⁷ and, consequently, induce them to devise experimental areas in their laboratories for testing some of these schemes at various points at which they might be amenable to experimental laboratory tests.⁸⁻¹⁰ The degree of success of a variety of these experiments has, in turn, modified the original constructs, and even led to new experiments, both in biology and in chemistry, particularly the latter.

Up until now, all our knowledge about the nature of the extra-terrestrial universe has been based entirely upon the information that has been carried to us by electromagnetic radiation (until recently only visible light, now we may add radiofrequency waves) from elsewhere. However, we are about to begin (or, in fact, have already begun) an exploration of the space beyond the reaches of the earth's atmosphere and will soon be exploring not only our own satellite, the Moon, but our two nearest planetary neighbors, Venus and Mars. Here we will be able to get direct first-hand information not only about the nature of the materials of which these objects are constructed, but also about the possible existence on their surface either of matter which we would be willing to call living, or of matter which might have ultimately given rise to living things, or be the residue of living things. This will add immeasurably not only to our intellectual horizons but directly to the knowledge of the nature of the terrestrial organisms as well. We are even beginning to discuss seriously and make a few small attempts at communications with extraterrestrial organisms who might have not only our minimal power of understanding but perhaps even powers far beyond those which we know.¹¹

It therefore seems appropriate to say a few words both about the present state of our knowledge of chemical evolution on the earth and the generation of molecular communities which give rise to terrestrial organisms, as well as what little we know of the existence of corresponding organisms elsewhere.

TERRESTRIAL CHEMICAL EVOLUTION

What Is a Living System?

In any discussion of such a broad, all-encompassing subject as this we are always faced with the problem of trying to define the material system to which we are willing to attribute the adjective "living." Personally, I feel that this has a certain degree of subjective arbitrariness about it, since there are those who would be willing to allow the use of this term for systems which would not be acceptable to others. This peculiar characteristic of the problem immediately allows us to recognize that the qualities, or properties, which we require of a material system are of the nature of a continuous aggregation in time along which no sharp line of demarcation need necessarily exist. Rather than try to define that particular concatenation of properties of a molecular system which might be acceptable to everyone as living, I would rather recognize the difficulty of satisfying everyone, and simply take two of the qualities which everyone will agree are certainly basic attributes of a living system and try to describe the sequence of events which might have produced them from nonliving origins.

These two processes which I think most, if not all of us, would agree upon as being perquisites of present-day living systems are (1) their ability to transfer and transform energy in a directed way and (2) their ability to remember how to do this, once having learned

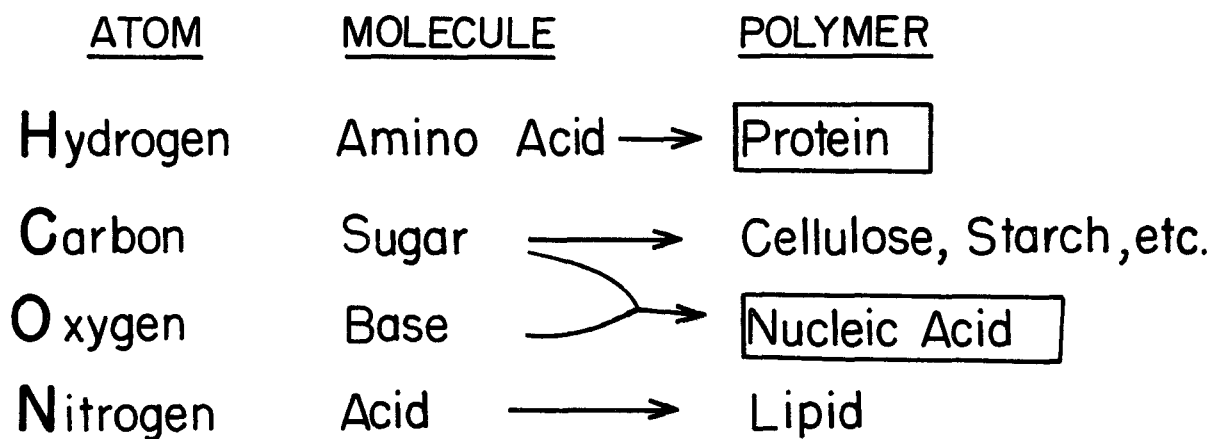
it, and to transfer or communicate that information to another system like itself which it can construct. Here we have, then, two of the principal problems of the biologist trying to understand a living organism in molecular terms. These are, restated: (1) The transfer and transformation of energy and (2) the communication and transformation of information. In the larger sense, I suppose, the second ability includes the first. The genetic information contains not only the directions for the construction of new organisms but for their function as well, and it is this function which is largely a matter of energy transfer and transformation.

Molecular Construction

In any case, the materials of which the living organism is constructed are known to us (or at least a good many of them are), and one of the characteristics of these materials is the essential requirement that they be constituted, at least in part, of polymeric molecules in order that the information storage and transfer be possible. The energy transformation as well seems dependent upon such macromolecular, or pseudo-crystalloidal, structures. Our evolutionary problem can now be defined in molecular terms as the devising of processes which will not only give rise to the simple molecular structural components of living things and, in addition, to macromolecules associated with them, but to their functional relationships, that is, energy transformation relationships, as well.

The most common elements of the universe, namely, hydrogen, carbon, oxygen and nitrogen, are also the most common ones in terrestrial living organisms, and some relationship between these atoms, the biologically important molecules and the polymers derived from them is shown in Figure 1. The chemical bonds which must be created in order to manufacture the simple molecules required for the construction of living organisms, such as amino acids, sugars, purine-pyrimidine bases, fatty and hydroxy acid, and the like, involve a wide variety of types (see Figure 1 and Figure 3). These include C-H, N-H, O-H, C-N, C-O, C-N, C=O, and perhaps other less widespread types. The step from the simple molecules to the polymers appears to be primarily of a single type, namely, the formation of either a C-O or C-N (and possibly a P-O) bond with a concomitant loss, or elimination, of a water molecule; we shall come back to this remarkably uniform reaction later.

The catalytic and energy transferring functions which today are so highly efficient were presumably evolved in the same molecules and by similar mechanism from the very primitive energy transferring and catalytic functions of the primeval molecules and ions present in the formation of the earth itself.¹²



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Figure 1. Schematic representation, in chemical terms, of the set of transformations which have to be accomplished from the atoms to produce the structure of the cell.

The Time Scale and the Starting Material

We must now turn to the question of the starting material that was available to us and the time available to achieve the transformations from that starting material into the forms we now recognize.

The time available since the formation of the earth seems to be something of the order of 4.5 to 5 billion years, and the logarithmic chart, with some bench marks on it, is shown in Figure 2. It is interesting to note that the period marked Chemical Evolution, presumably beginning with the formation of the earth in its present shape, and the period marked Organic Evolution, beginning with the appearance of molecular systems which we would call alive, are shown to overlap in the region of 2 billion years ago, roughly halfway through the age of the earth. An interesting calculation can be made concerning the two stages of evolution which might be separated at such a point. The earliest stage of Chemical Evolution leading up to the appearance of the first unicellular organisms would thus occupy some 2.5 billion years. The climb from the primitive unicellular organisms to the modern multicellular organisms required the remaining 2 billion years.

There is now more reason for this particular division than was originally at hand when it was made. It now appears that unicellular organisms resembling blue-green algae in form have been found in strata whose age is not less than 1.7 billion years.^{13, 14}

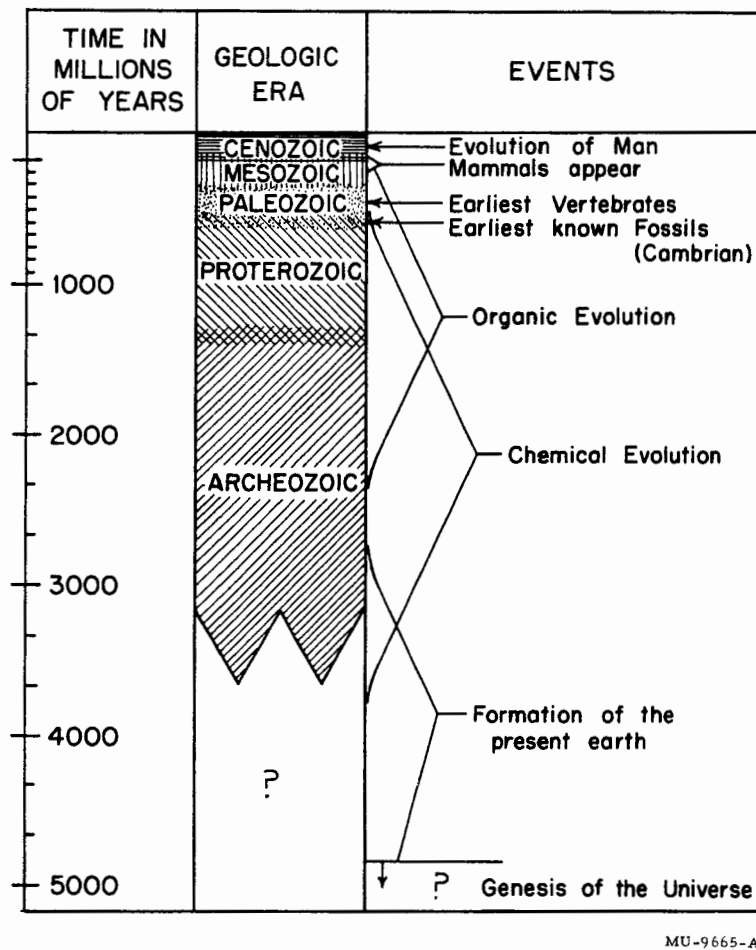


Figure 2. Time scale for total evolution.

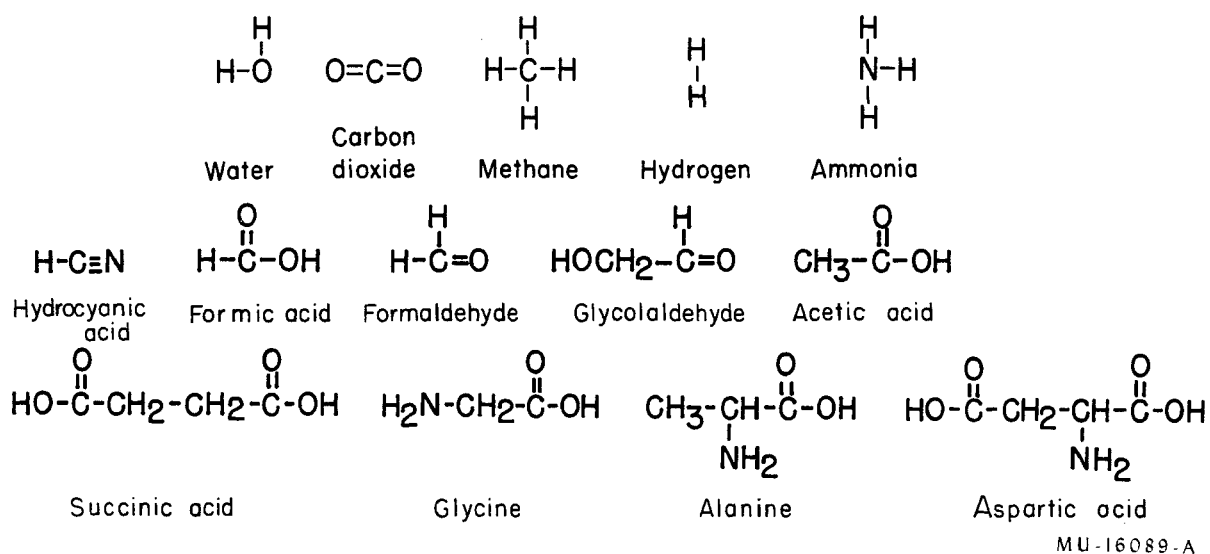
An estimate of the complexity of the unicellular system might be made in terms of the number of molecules that have to be organized to produce one. Roughly this amounts to 10^{10} molecules for a cell of approximately one micro diameter. Not all of these molecules are different, that is, some of these 10^{10} molecules would be made up of a much smaller number of different varieties. A similar calculation for the next transition from the unicellular level to the intelligent organism such as man gives a corresponding number of cells in the whole organism, again 10^{10} . So it is not surprising that the time required to organize 10^{10} molecules into a single cell and the time to organize 10^{10} cells into a full-fledged man should have been roughly the same order of magnitude.

The evolution of highly efficient mechanism for the storage and transfer of information (and energy conversion) took place during the first phase of this evolutionary time sequence and was dependent upon the properties inherent in the macromolecules (nucleic acids, proteins) which appeared during that period. Similarly, the evolution of efficient mechanisms for the control and ordered development of the information contained in the transferred molecules was based upon the properties of the information transferring system itself, and probably took place largely during the second period, giving rise to all the phenomena of growth and differentiation of multicellular organisms as we know them

today. This requires, of course, that such control mechanisms were already inherently present, even in the unicellular organisms.

While we have developed, in the past decade, a more or less consistent understanding of the nature of information transfer on a molecular basis, we are only just beginning to understand the way in which that information manifests itself in growth, development and differentiation of cells and tissues on a molecular basis. This seems to be a problem of molecular communication of the nucleus of the cell (the information storage vault with its environment through the intermediary of the cytoplasmic constituents (see Figure 17). It is quite obvious that an understanding of the mechanism of this communication problem is of great importance to us for practical as well as philosophical reasons.

We now return to the question of the nature of the actual organic starting materials from which all this was derived. Perhaps the simplest way to begin will be to recognize that the primeval earth had accumulated in it, or on it, the very same organic materials which are widespread throughout the solar system and the galaxy as well, namely, the very simplest compounds of carbon, hydrogen, oxygen and nitrogen.^{15, 16} It is presumed that these were largely dominated by hydrogen and, therefore, were generally in their most reduced forms. These materials are represented by the molecules in the top row of Figure 3 and the molecules with which we have to work are thus methane, ammonia, water, and a large amount of hydrogen, and perhaps some carbon monoxide and carbon dioxide.



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Figure 3. Primeval and primitive organic molecules.

Energy Sources

In order for these molecules to undergo transformations, a source of energy must be provided, and here we have a wide variety to choose from. The sources of energy and their possible availabilities are shown in Table 1. The principal source of energy that could be used by such

TABLE 1—ENERGY AVAILABLE FOR SYNTHESIS OF ORGANIC COMPOUNDS

| Source of Energy | Energy (in 10^{20} cal/yr) |
|--|---------------------------------|
| Decay of K^{40} in earth's crust at present | 0.3 |
| Decay of K^{40} in earth's crust 1.3×10^9 years ago | 0.6 |
| Decay of K^{40} in earth's crust 2.6×10^9 years ago | 1.2 |
| Ultraviolet light of wavelength below 1500 Å | 0.08 |
| Ultraviolet light of wavelength below 2000 Å | 4.5 |
| Ultraviolet light of wavelength below 2500 Å | 30. |
| Lightning | 0.05 |

an aggregation of molecules seems to be light of wavelength of 2000 Å or shorter. Radioactivity in the earth's crust, electric discharges in the atmosphere and cosmic radiation are secondary and tertiary sources of energy for these transformations as well.

At this stage in our knowledge of the chemical transformations induced by such high energy radiations, including ultraviolet, there does not appear to be any marked systematic difference between the products from one type of high energy radiation and those of another, at least among these. And so we will call equally upon experiments which have been performed with all of these energy sources.

Initial Transformations

The earliest experiments designed to test the notions here introduced were done using a high energy alpha particle beam on the cyclotron and were reported in 1951.⁸ Here it was shown that carbon dioxide dissolved in water and irradiated in the presence of ferrous iron and hydrogen could produce a variety of reduced carbon compounds, including formaldehyde and formic acid.

Since then similar experiments have been performed with other energy sources with the same starting materials and demonstrating not only that particles but ultraviolet light¹⁸ and gamma rays¹⁹ can produce reduced carbon under these conditions. The next major step was taken when Miller introduced ammonia into these reaction systems, together with reduced carbon in the form of methane. Here the energy source was electric discharge, and Miller was able to demonstrate very clearly the appearance of amino acids as major products under such conditions.^{9, 10} Ultraviolet light has been used for a similar demonstration.²⁰

The presence of HCN was inferred from the appearance of amino acids in Miller's early experiments. Its quantitative demonstration was achieved in an electron bombardment of a similar mixture of methane, ammonia, hydrogen and water.²¹ The importance of HCN as an early product in these reactions arises from the recent demonstration of the formation of adenine when an ammoniacal solution of HCN is allowed to stand.^{22,23} A variety of other biologically important simple molecules has since been demonstrated to arise in solutions of ammonium cyanide under very mild conditions.^{24,25} Thus we see that the molecules of the primeval earth shown in the first row of Figure 3 can very readily be -- and in fact have been -- transformed into the primitive organic molecules shown in the second row, by any of the energy sources which we know to have been available.

Not only can we generate important biological molecules, such as amino acids and purine and pyrimidine bases, from HCN and others of these simple molecules by base catalysis, but the sugars themselves are now very easily derivable, again by base catalysis, from the formaldehyde generated by the methods just described. It has long been known that the treatment of aqueous formaldehyde with lime or limestone will produce a mixture of carbohydrates which has been given the name formose (figure 4). More recently, this reaction has been examined with modern analytical tools and the preference for certain sugars and sugar configurations has been demonstrated.^{26,27} That such four-, five-, six-,

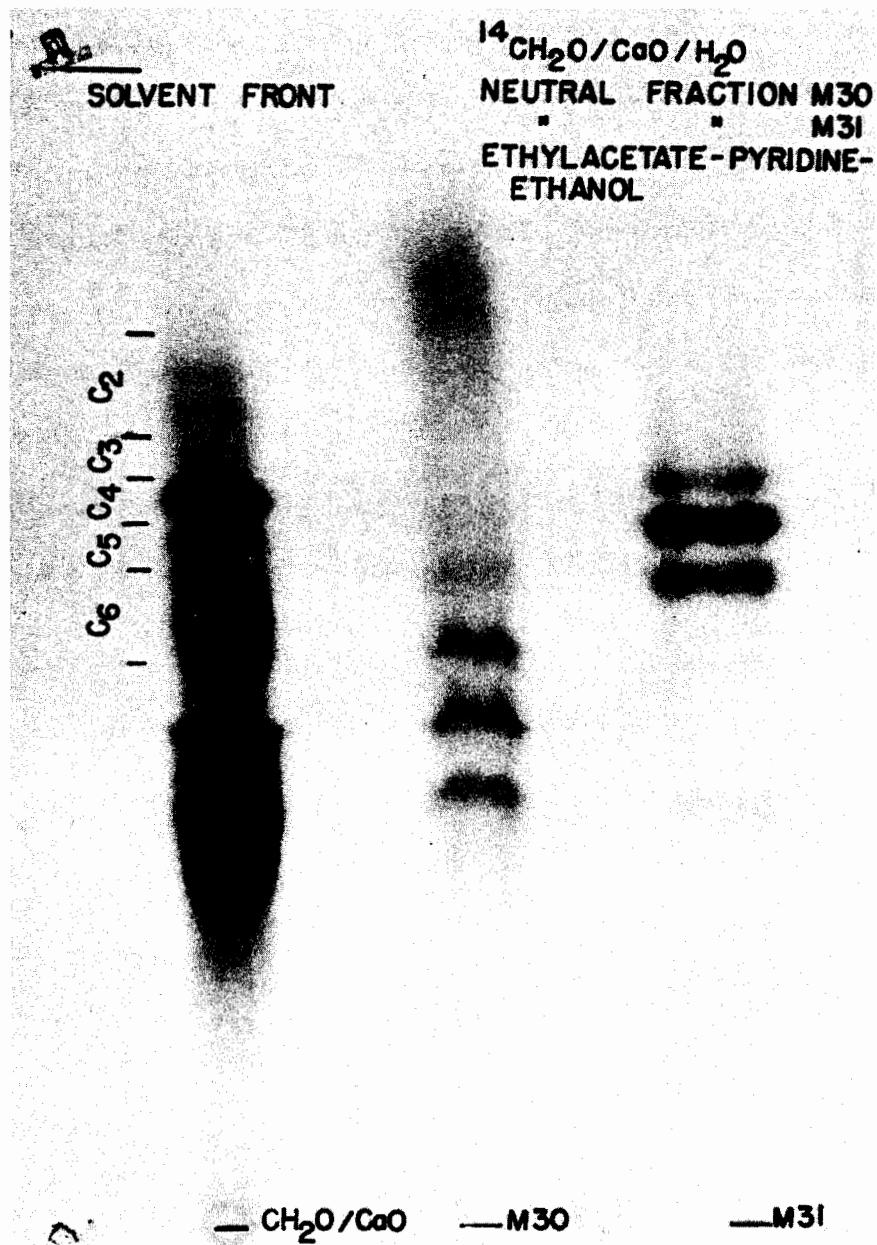


Figure 4. Route to carbohydrates as a result of treatment of formaldehyde with lime or limestone.

and seven-carbon sugars may be generated directly by electron bombardment of the methane-ammonia-water-hydrogen system was shown by comparison of radioautographs of the products of such an irradiation using $C^{14}H_4$ with the products of lime treatment of formaldehyde is shown in Figure 5.²¹ That a wide variety of other compounds are also formed under these conditions has been demonstrated and is spectacularly evident in a radioautograph of these products shown in Figure 6. Most of these discrete spots have not yet been identified. The analysis of such a mixture is given in Table 2. A distribution of products resulting from the sparking of methane-ammonia-water-hydrogen mixture taken from Miller²⁸ is shown in Table 3.

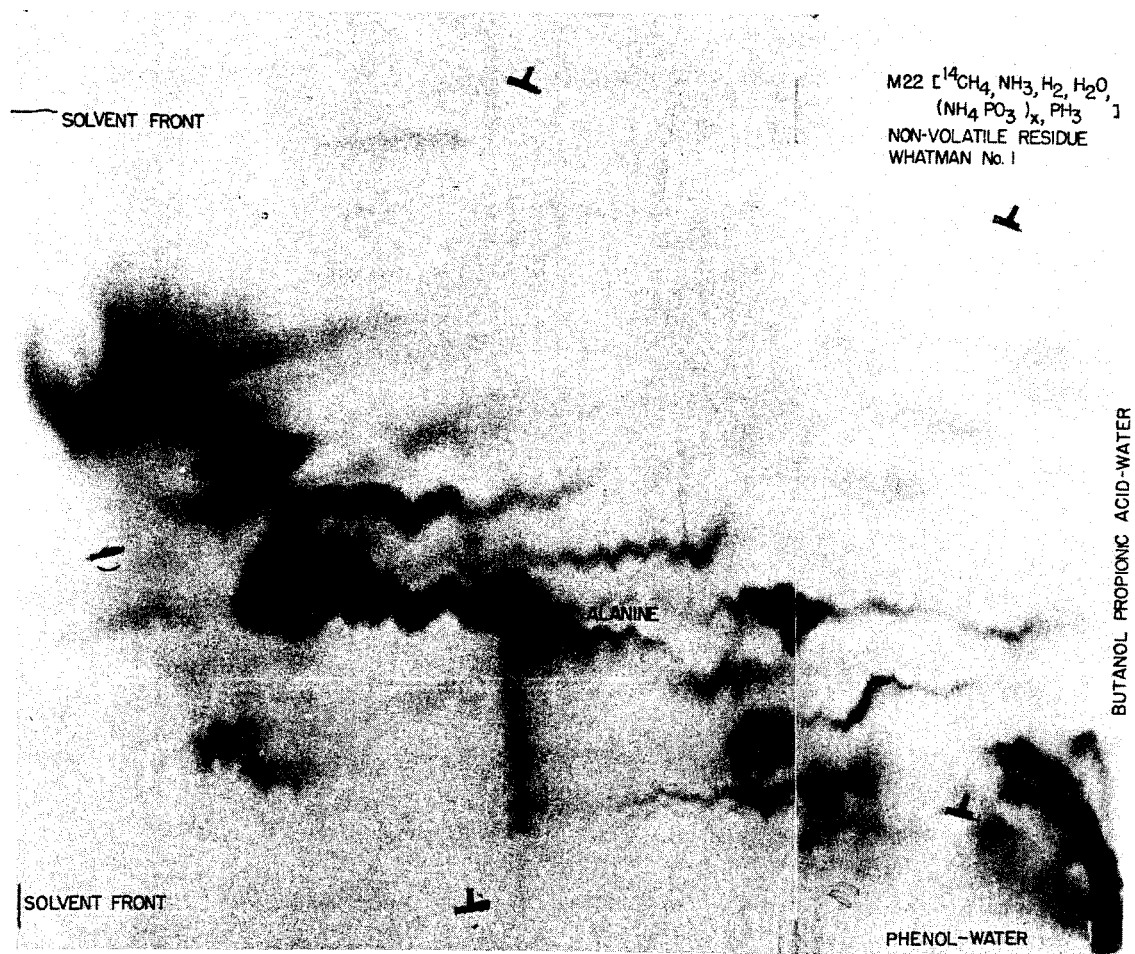
TABLE 2--IDENTIFICATION OF COMPOUNDS FROM IRRADIATION
EXPERIMENT FROM C^{14} -LABELED METHANE,
AMMONIA, AND WATER

| Experiment M22 $^{14}CH_4$, NH_3 , H_2O , PH_3 (NH_4PO_3) ₃ | | | |
|--|---|--------------------------|---------------------------------------|
| Acid fraction | = | 45.5% | separation on Dowex 1 and Dowex 50 |
| Basic fraction | = | 17.44% | |
| Nonionic fraction | = | 21.3% | |
| HCN | = | 0.45% of total | |
| Adenine | = | 0.203% of basic fraction | |
| | = | 0.034% of total | |
| 5-Aminoimidazole-carboxamide | = | 0.105% of basic fraction | |
| | = | 0.018% of total | |
| Lactic acid | = | 2.21% of acid fraction | |
| | = | 0.99% of total | |
| The two unknown other dominating acids (not including lactic) account for 29% and 17.8%, respectively, of the acid fraction. | | | |
| Glycine | = | 0.2% of basic fraction | |
| | = | 0.03% of total | |
| α -Alanine | = | 1.07% of basic fraction | |
| | = | 0.18% of total | |
| Aspartic acid | = | 0.2% of basic fraction | |
| | = | 0.03% of total | |
| The two unknown (not urea or guanidine) dominating basic compounds (ninhydrin positive) account for 20.9% and 11.9% of the basic fraction. | | | |



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Figure 5. Neutral fraction of experiments M30 and M31 in comparison to "formose" from formaldehyde and CaO. Solvent: ethyl acetate-pyridine-water 10:3:3.



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Figure 6. Radioautograph of chromatogram of nonvolatile residue of experiment M22.21

Table 3. Yields in moles ($\times 10^5$) from sparking a mixture of CH_4 , NH_3 , H_2O and H_2 . 710 mg of carbon was added as CH_4 .

| | | | |
|--------------------------------|-----|----------------------------|-----|
| Glycine | 63 | Succinic acid | 4 |
| Glycolic acid | 56 | Aspartic acid | 0.4 |
| Sarcosine | 5 | Glutamic acid | 0.6 |
| Alanine | 34 | Iminodiacetic acid | 5.5 |
| Lactic acid | 31 | Iminoacetic-propionic acid | 1.5 |
| N-Methylalanine | 1 | Formic acid | 233 |
| α -Amino-n-butyric acid | 5 | Acetic acid | 15 |
| α -Aminoisobutyric acid | 0.1 | Propionic acid | 13 |
| α -Hydroxybutyric acid | 5 | Urea | 2.0 |
| β -Alanine | 15 | N-Methyl urea | 1.5 |

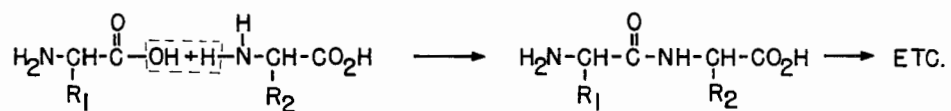
It is thus quite clear that any of these high energy radiation sources operating on the primeval molecules of the earth's surface can and do produce the simple organic materials, including many new carbon-carbon bonds, from which the polymeric materials may themselves ultimately be derived. These simple materials include amino acids, carbohydrates, purine-pyrimidine bases, fatty acids, hydroxy acids, alcohols and the like. It is from these, now, that we must begin to build both the more selective catalytic agents required for the more efficient energy transformation as well as the macromolecules which help in this process and which are essential for information storage and communication.

The evolution of catalytic systems, such as the iron porphyrins, has been discussed in some detail elsewhere.⁷ Suffice it to say that there is ample evidence for the gradual selection by autocatalytic mechanisms of increasingly more efficient catalytic systems. Notable among these is, of course, the ability of iron in various chemical combinations to act as a catalyst for a wide variety of redox reactions. The evolution of the iron porphyrins undoubtedly took place by an autocatalytic response to the need for such redox catalysts, particularly resulting from the generation of hydrogen peroxide, and possibly oxygen, by the high energy radiation decomposition of water, and the escape of hydrogen.

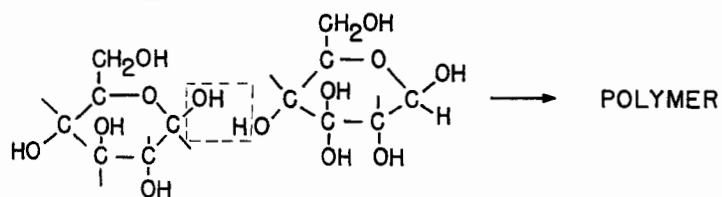
Polymerization

One of the outstanding characteristics of living organisms has often been described as the high degree of organization which they show, and this particularly in terms of the specific macromolecules of which they are constructed. The formation of all of these macromolecules, specified in the polymer column of Figure 1, involves the same reaction, namely, the condensation of two simple molecules with the elimination of water between them. When such molecules are polyfunctional, that is, have two functional ends, they can do this at both ends. It is clear that a polymer results. The essential feature of each of these reactions is shown in Figure 7. The formation of lipid indicated on Figure 1 but not shown on Figure 7 is a simple esterification reaction involving the elimination

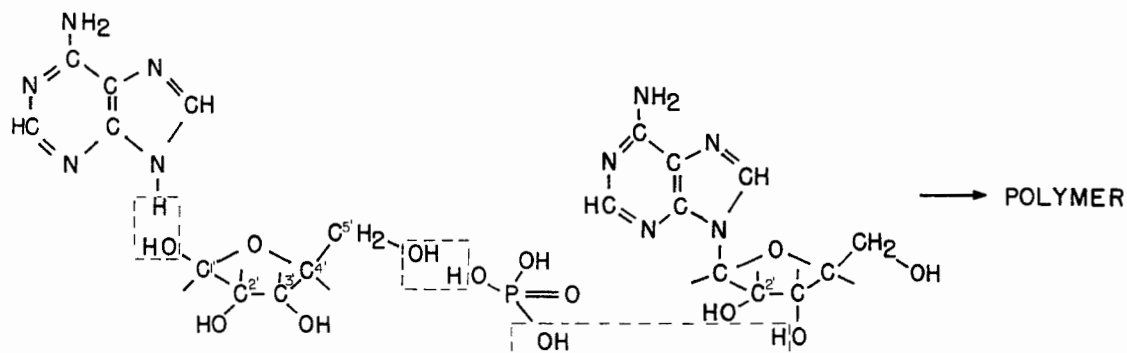
PROTEINS



POLYSACCHARIDES



NUCLEIC ACIDS (3 STAGES) RNA SHOWN - DNA LACKS OH ON 2' POSITION



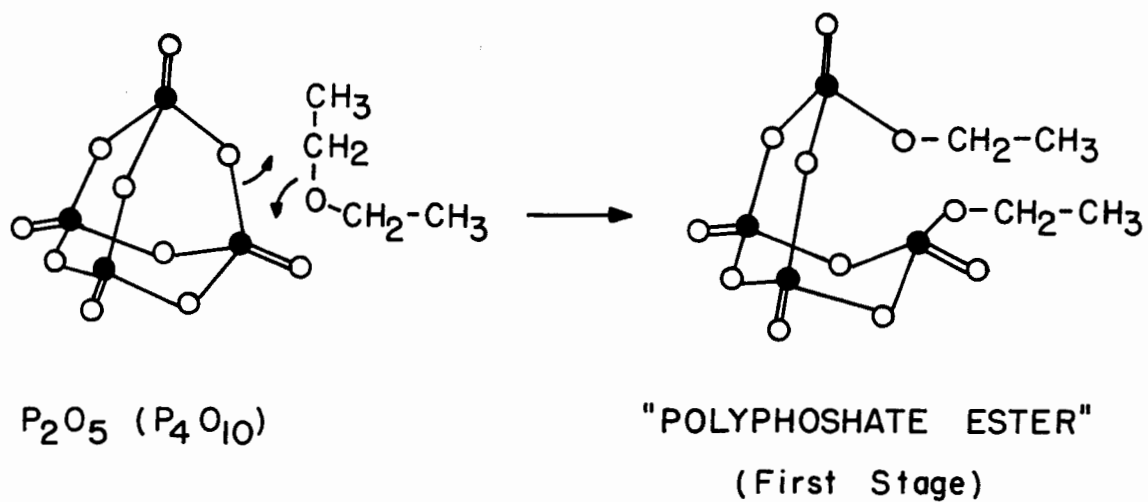
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Figure 7. Dehydration reactions leading to biopolymers.

of water between a fatty acid carboxyl and glycerol alcohol group. We have already seen how the monomeric materials required for the construction of these polymers may be formed.

In recent years it has been possible to demonstrate the direct non-enzymatic dehydration reaction in all of these systems to produce polymers. At first these reactions were carried out in nonaqueous media, but more recently they have been successful even in water, and it is the reagents which are capable of doing this which we must seek, since these are the very reactions which today are functioning in the living organism.

The principal agent for these dehydration reactions in the modern organism is the pyrophosphate linkage (at least this is the one we know today), generally in the form of adenosine triphosphate. The accumulation of polyphosphoric acid and its derivatives in simple organisms such as algae^{30,31} and yeast²⁹ is also very suggestive. Some years ago Fox was able to demonstrate that the formation of polypeptides in a mixture of molten amino acids with excess glutamic acid was enhanced by the presence of phosphoric anhydride.^{32,33} More recently, a still milder set of conditions was devised by Schramm, which was able to accomplish this dehydration, using a derivative of phosphoric anhydride made with diethyl ether.³⁴ This reagent, whose structure is as yet not known, might very well be a di- or tetra-ethyl ester of tetrapolyphosphate derived from P_2O_5 (P_4O_{10}), as shown in Figure 8. Schramm has used this reagent



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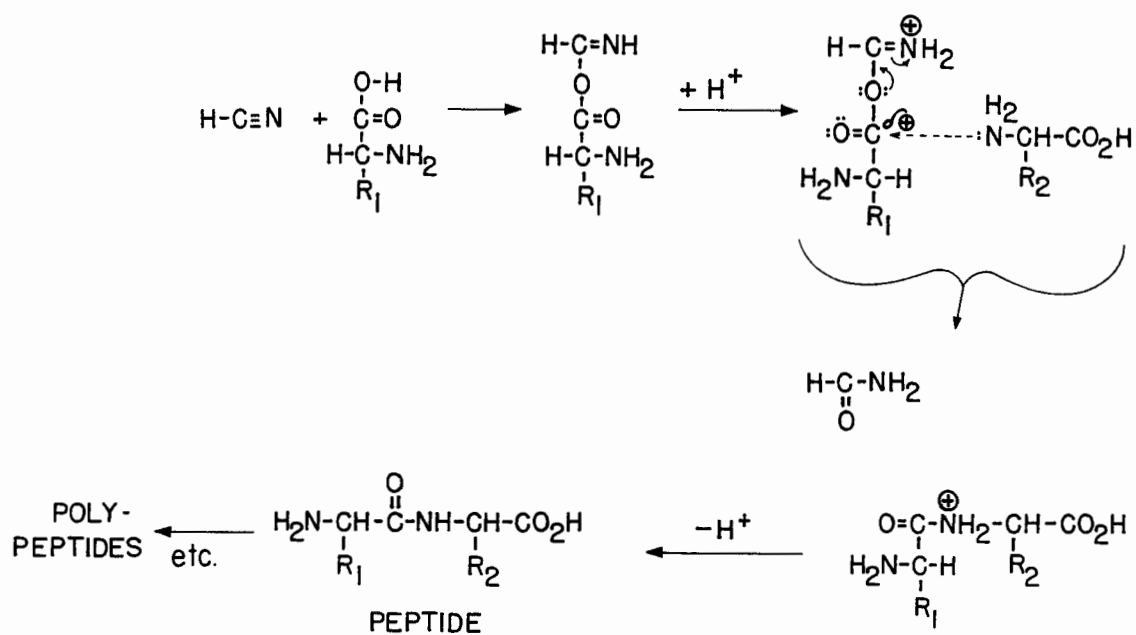
Figure 8. Formation and possible structure of "polyphosphate ester."

not only to make polypeptides from amino acids but to dehydrate simple monosaccharides to produce polysaccharides and, finally, to induce a sequence of three dehydration reactions, shown in the bottom of Figure 7, leading from the purine base, into sugar, all the way to the polynucleotides. As yet, the high polymers and the efficient reactions have only been achieved in nonaqueous media such as dimethyl formamide.

Still another route to polymers in aqueous solution has recently been demonstrated by Markham and his associates for polypeptides.²⁴ Although the polymerization of HCN in an aqueous ammoniacal solution has long been known, it remained for the stimulus of questions such as the ones we have discussed to show not only the presence of purine and pyrimidine bases, as well as amino acids, in such a reaction mixture, but still more recently the demonstration of polypeptides as well.^{23, 24, 35} That this was indeed a polymerization of preformed amino acids was demonstrated by adding labeled amino acids to the polymerization mixture and finding them in the polymers.

We can thus formulate still another dehydration mechanism involving the use of HCN as the dehydrating agent which would be analogous to the use of the carbodiimides for the same purpose (Figure 9).³⁶ It will be interesting to watch the development of our knowledge of modern biological systems to see if any such dehydration mechanisms as this are found among them.

The primitive origin of these dehydrating agents is readily understood. We have already seen that HCN is one of the principal products of the interaction of high energy radiation with the primeval terrestrial atmosphere. It is also well known that any aqueous phosphate solution which is allowed to dry at temperatures approaching 100° C gives rise to the formation of a polyphosphate which itself is not extremely rapidly hydrolyzed upon redissolving. It is this resistance to immediate hydrolysis with water of both the pyrophosphate and the carbon-nitrogen multiple bond which gives rise to their specific ability to couple monomers with the absorption of water.

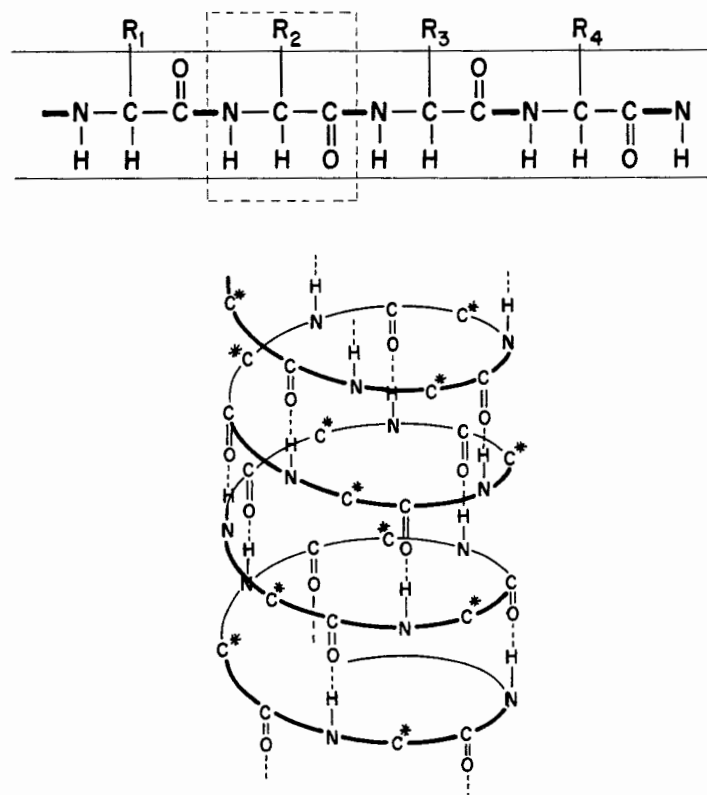


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Figure 9. Possible mechanism of peptide formation with HCN as dehydrating agent.

GENERATION OF ORDER AND NEW INFORMATION

Perhaps one of the most outstanding characteristics of the two biopolymers with which we are dealing, namely, the proteins and the nucleic acids, is the fact that once having been put together they have in their very structural relationships the intrinsic ability to arrange themselves in a highly ordered array. This arrangement is completely analogous to the crystallization of small molecules out of solution. However, in the case of the polymers it does not involve a precipitation from solution but simply an arrangement in a very highly ordered array of the long polymeric chain in which the individual units stand in a very specific and pseudocrystalline array with respect to each other. In the case of the polypeptide this array tends to be a helical one which is stabilized, at least in part, by the formation of hydrogen bonds between the amide hydrogen and the amide carbonyl several peptide residues removed.³⁷ This structure is shown in Figure 10, and the demonstration that this structure is spontaneously formed may be made in a variety of ways. One such demonstration may be done with a synthetic polymer whose microstructure is completely known, namely, polyglutamic acid. Here it is easy to show that when the carboxyl groups at the ends of the side chains, represented in Figure 10 by R_1 , R_2 , etc., are all ionized by adjusting the pH to something above 7, the electrostatic repulsion of these charged ends is sufficient to overcome the organizing force of the helix, and the

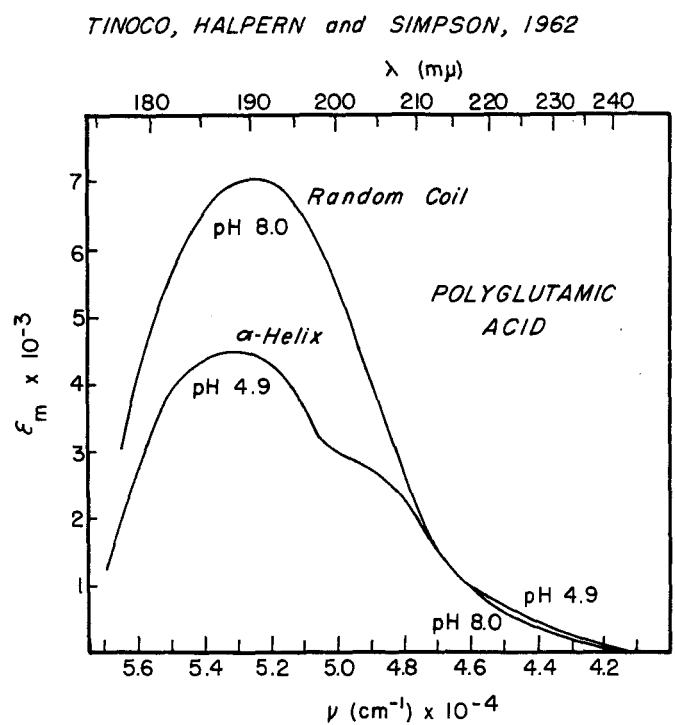


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Figure 10. Protein structure.

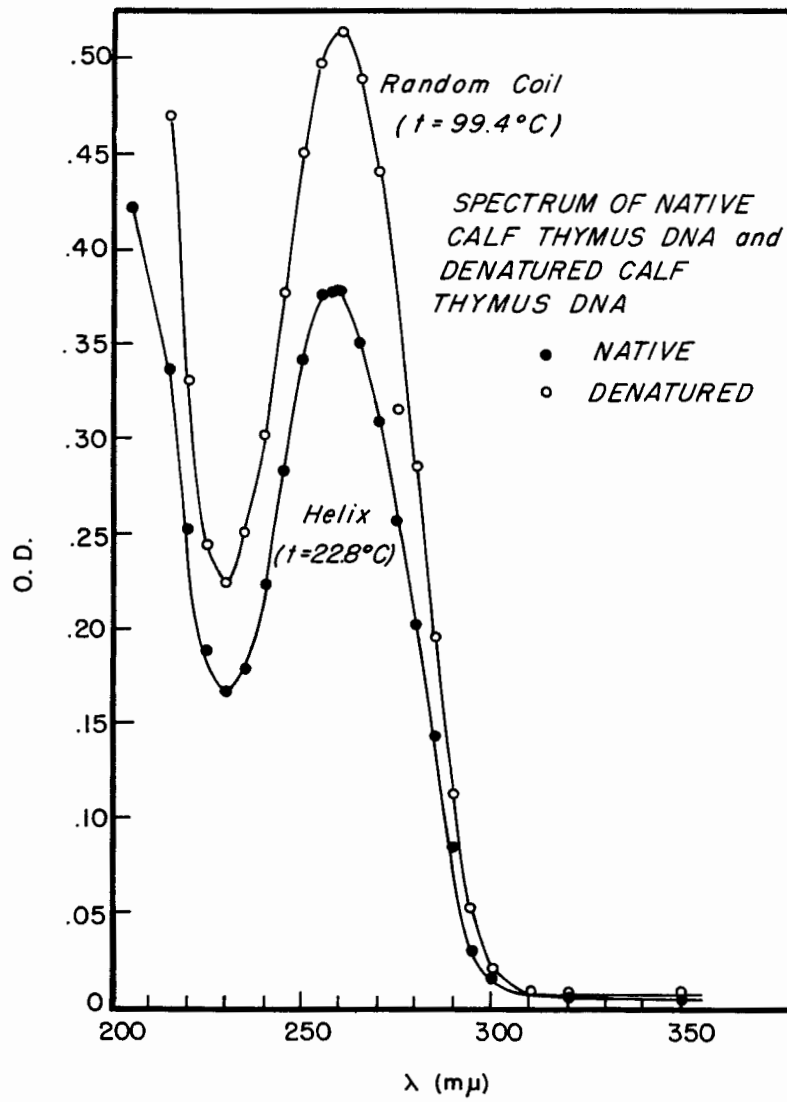
helix is destroyed. When the side chain carboxyls are neutralized, at pH's below 5, the helix can reform, and these two states are reflected in a variety of properties, among them the absorption spectrum (Figure 11).³⁸ When the helix is formed, the peptide linkages interact with each other, giving rise to decrease of absorbance and splitting into two bands, which show very clearly in the curve below pH 5.

A similar molecular crystallization phenomenon occurs in the polynucleotides and may be demonstrated again by a wide variety of methods, of which I will here only use one, namely, the change in absorption spectrum when the polymer is ordered, as opposed to when it is disordered. Here the transition between order and disorder is also reversible and has been achieved by a change in temperatures (Figure 12). The curve at 99.4°C shows the absorption primarily of the purine-pyrimidine bases when there is relatively little interaction between them, as would be the case in the bases alone. When the temperature is lowered, the helical configuration is reformed, and the absorption decrease is shown by the absorption at 22.8°C. This decrease in absorption upon assuming the helical configuration, due to the interaction of the bases with each other lying in parallel planes, is known as hyperchromism and has recently been used as a measure of the degree of order in a particular sample. The polynucleotide system, however, has in it not only the tendency for intrinsic order in the form of the helix, but because of the nature of the bases and the geometry of their hydrogen bonds, inter-



MU-27653

Figure 11. Absorption spectrum of polyglutamic acid in both helical and random coil forms.



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Figure 12. Hyperchromism on nucleic acid.

action between them gives rise to a specificity in the pairing of the bases as shown in Figure 13 in which thymine pairs with adenine and cytosine pairs with guanine. This base pairing specificity, together with the interactions responsible for the helical structure, give rise to the principle of complementary base strands of nucleic acid upon which the whole structure of bioreplication is based.^{39, 40} Thus in Figure 14 the strand on the left induces the formation of the complementary strand, on the right, which, in turn, gives rise to the original strand. This type of molecular communication can thus account for the reproduction of molecules belonging to the same class, such as chromosome duplication involves. This influence of a particular base sequence on its own replication has long since been demonstrated in the requirement of the enzymatic synthesis of deoxyribonucleic acid (DNA),⁴¹ for the presence of a primer DNA molecule which not only provides the information required for the synthesis of the new sequence but also catalyzes it.

A similar relationship has been demonstrated for ribonucleic acid (RNA) replication on a DNA template (messenger RNA).^{42, 43} In fact, the catalytic and information control of the polymerization of bases to produce a polynucleotide has even been demonstrated in the nonenzymatic polymerization of uridine phosphate in the presence of polyadenylic acid; this is shown in Figure 15.³⁴ Here, again, I think it is easy to see how primitive catalytic and information transfer systems on a molecular level may be evolved by a process

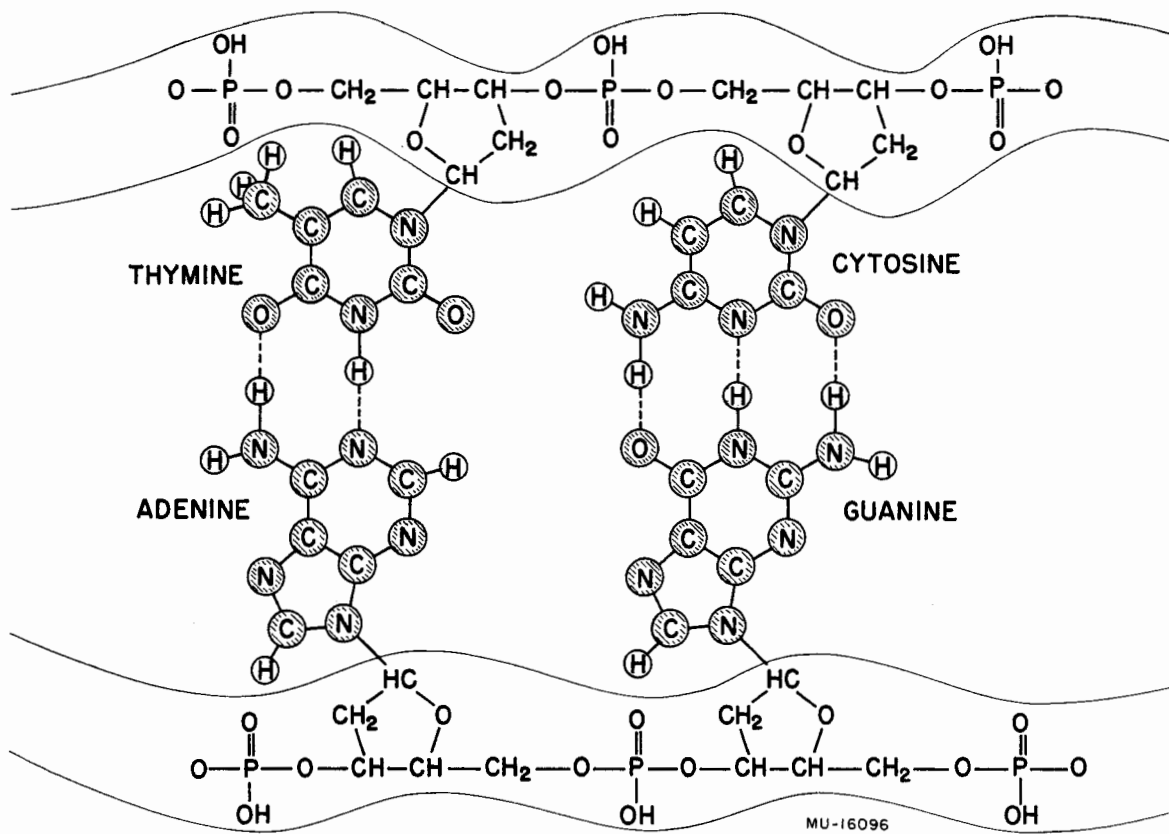
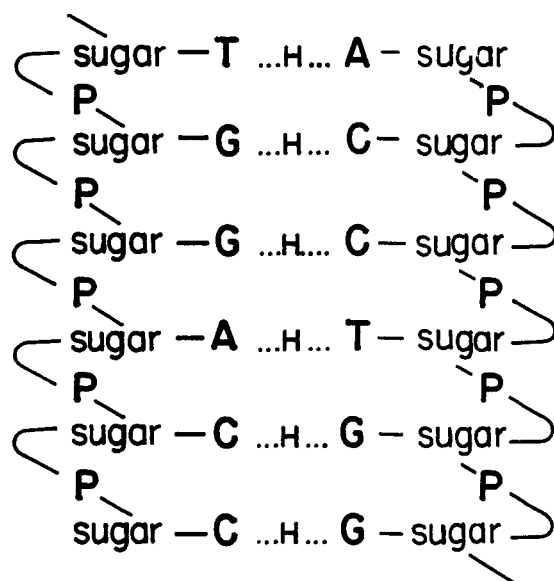


Figure 13. Molecular drawing of components of DNA.



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Figure 14. Base pairing for DNA replication and RNA template formation.

Schramm et al., 1962

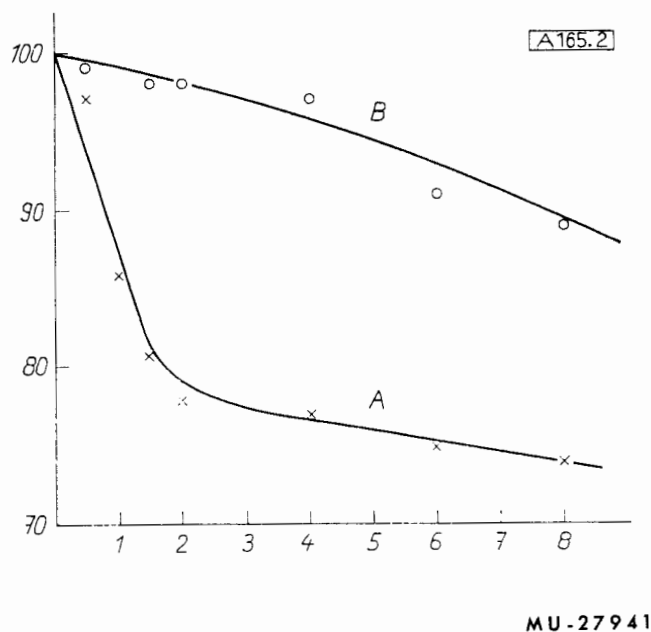


Figure 15. Polymerization of uridine monophosphate in the presence (A) and in the absence (B), of polyadenylic acid. (The decrease of free uridine monophosphate was measured chromatographically).

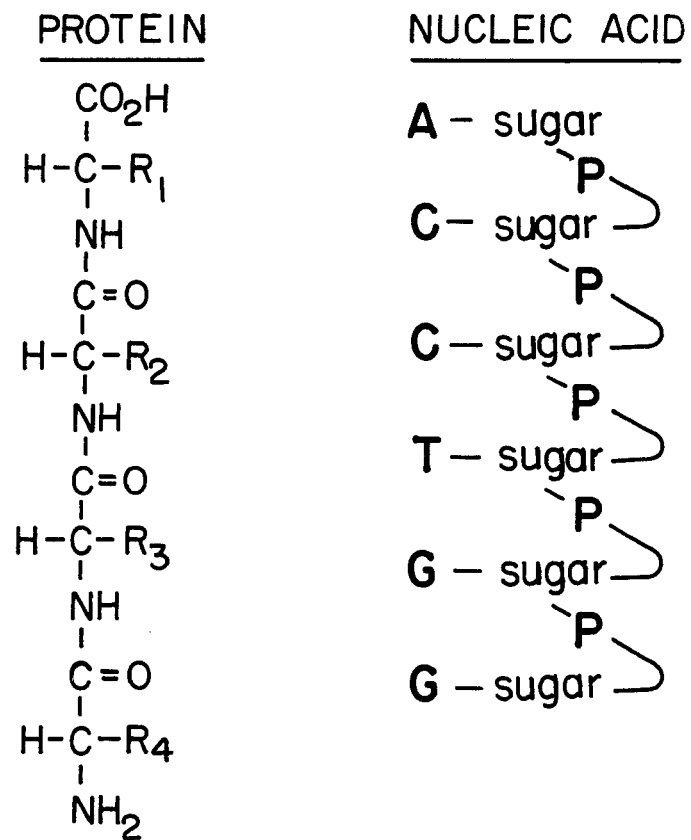
Abcissa: Time (hours)

Ordinate: % free uridine monophosphate (referred to the amount of starting material).

of molecular selection, just as we have suggested its occurrence for the energy transfer catalytic systems.

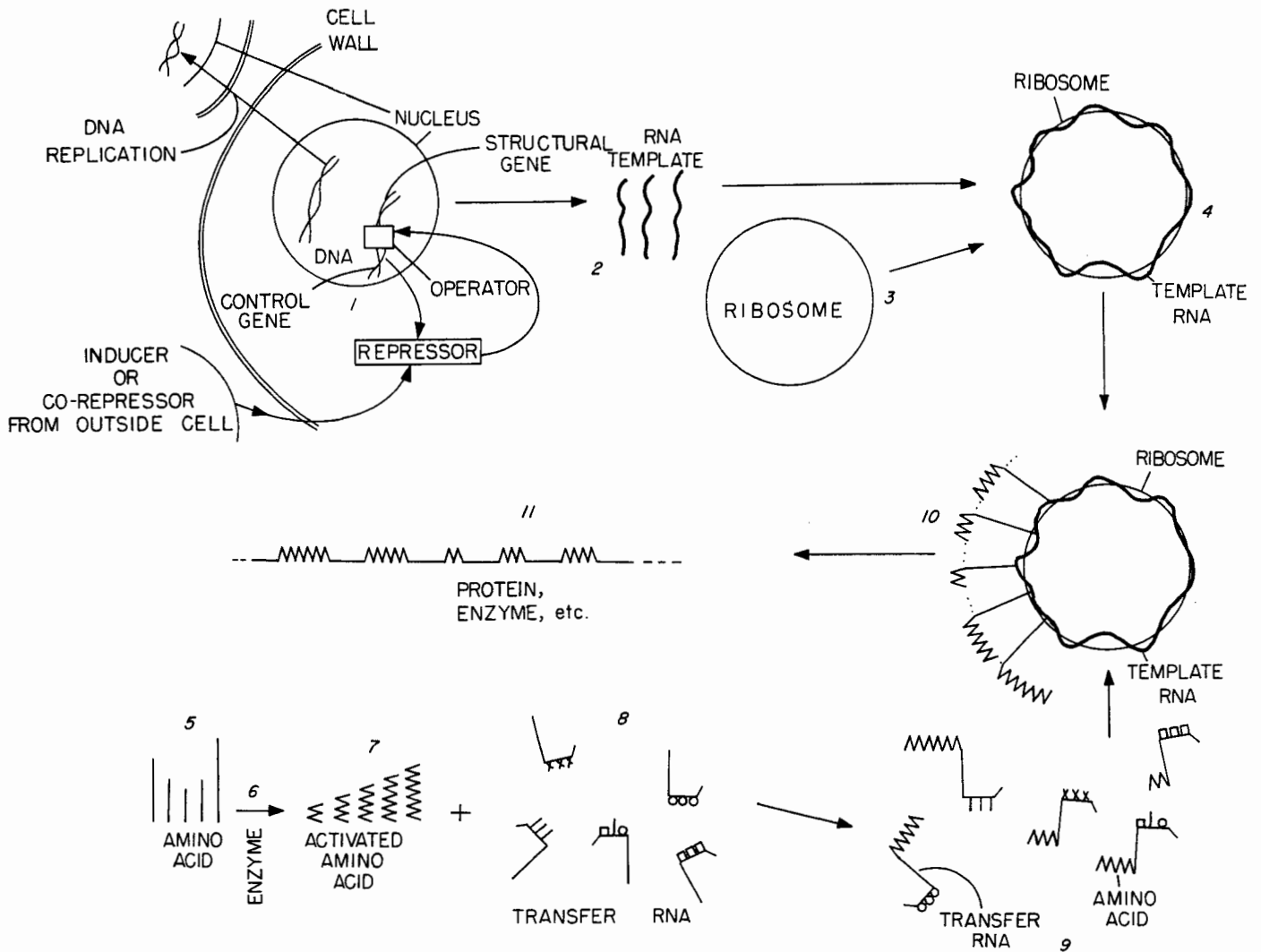
The question of the relationship between the linear sequences of bases in a nucleic acid and the linear sequence of amino acids in the protein, as shown in Figure 16, is still with us. However, a great deal of progress has been made toward the elucidation of that molecular communication problem in recent months.^{44, 45, 46} A sequence of events as it now seems to take place is illustrated in Figure 17 by the reaction sequences from 1 to 11. The essential recognition step which involves the cross-over between the two types of polymers is Step 6 in which the active amino acid is hung on one of the specific transfer RNA's, having a different and specific -- presumably three base -- sequence corresponding to each amino acid, as shown in Group 8 of Figure 17. All the remaining communication steps involve base pairing of either DNA or RNA.

We are only just now beginning to understand the mechanisms by which the nuclear DNA which gives rise to the messenger RNA (Step 2, RNA template, Figure 17) is controlled. This control mechanism is diagrammatically represented in the upper left hand corner of Figure 17, according to the theories of Jacob and Monod.^{47, 48} The essential feature here is the mechanism provided for the interaction of materials from outside the cell with the genetic apparatus in the nucleus via inducer or



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Figure 16. Structure of protein and nucleic acid.



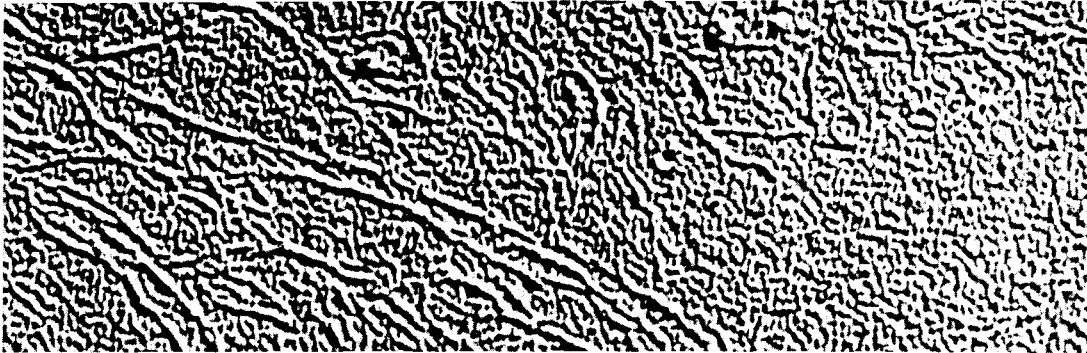
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Figure 17.

co-repressor acting with the repressor substance which appears in the cytoplasm. Presumably it is through such mechanisms as this that the first and obvious external effects of what appear to be genetically controlled processes may be found. It may be that the thalidomide effect on the growth and differentiation of human embryos as well as the more longstanding problems such as drug addiction and the long term effects of insecticides will ultimately be understood in these terms.

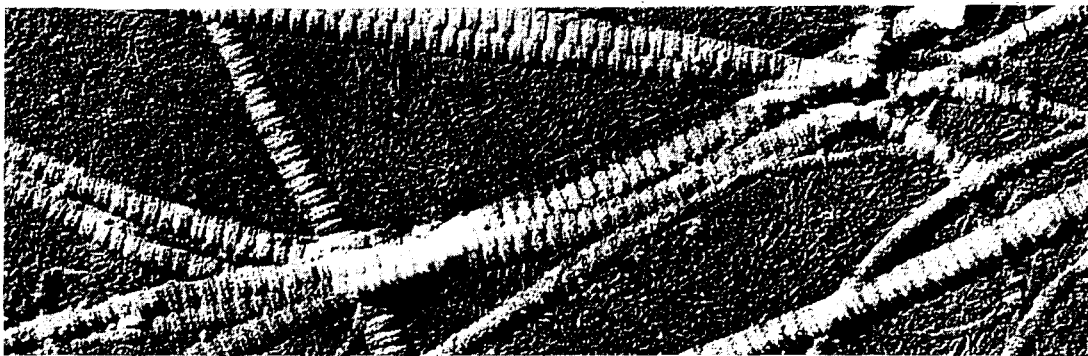
The Next Level of Organization

Just as the ordered array observed in the structure of the polymer was dependent upon the monomers of which it is made and their arrangement, so the order in which polymers may themselves be organized is built right into the structure of the polymers. Here, however, we are on less clearly defined chemical and structural grounds and much more has yet to be done before we will understand its detailed mechanisms. However, that such is the case is amply demonstrable. For example, a solution of protein molecules made from collagen can be reprecipitated by simply adjusting the medium to produce large aggregates of these molecules easily visible in an electron microscope which have a structure indistinguishable from the original collagen fibrils (Figure 18). Similar "crystallization" phenomena may be observed with other shaped molecules on a somewhat higher level; for example, the crystallization of viruses, both of the rod and spherical type.



FILAMENTS OF COLLAGEN, a protein which is usually found in long fibrils, were dispersed by placing them in dilute acetic

acid. This electron micrograph, which enlarges the filaments 75,000 times, was made by Jerome Gross of the Harvard Medical School.



FIBRILS OF COLLAGEN formed spontaneously out of filaments such as those shown *above* when 1 per cent of sodium

chloride was added to the dilute acetic acid. These long fibrils are identical in appearance with those of collagen before dispersion.

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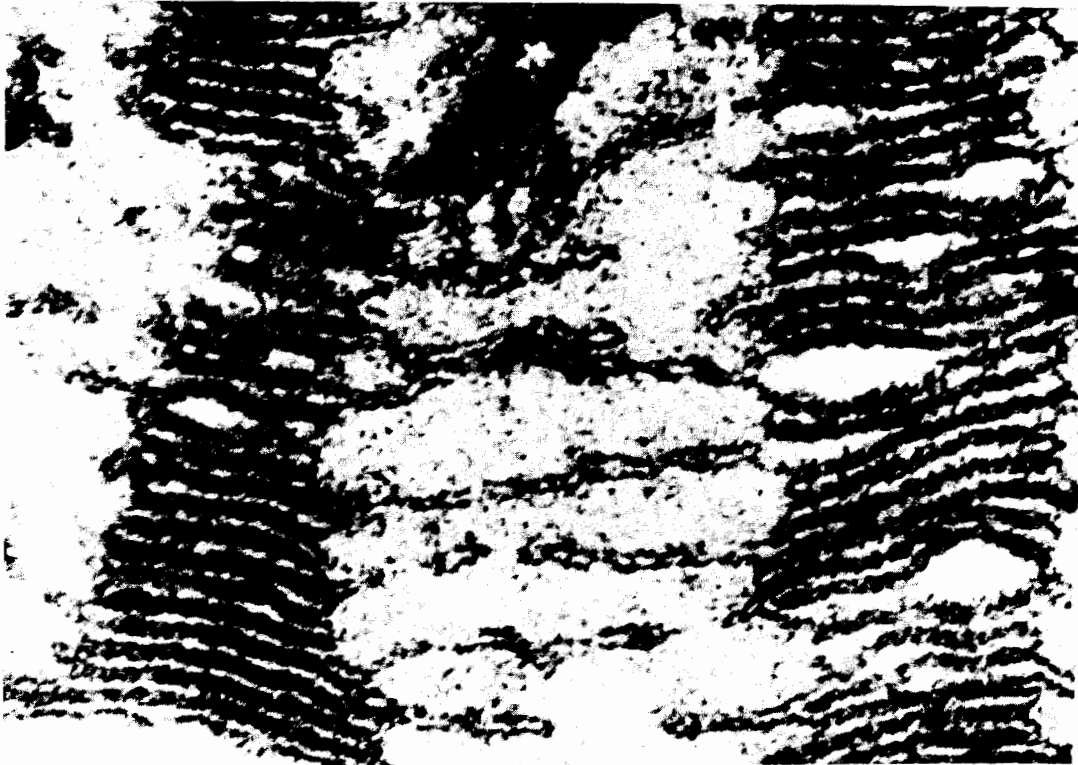
Figure 18. Structure of collagen. Top: filaments of collagen, a protein which is usually found in long fibrils, were dispersed by placing them in dilute acetic acid. This electron micrograph, which enlarges the filaments 75,000 times, was made by J. Gross of the Harvard Medical School. Bottom: Fibrils of collagen formed spontaneously out of filaments such as those shown above when 1% of sodium chloride was added to the dilute acetic acid. These long fibrils are identical in appearance with those of collagen before dispersion.

Something resembling this crystallization of spherical viruses appears to show in the visible structures which can be seen in the plant chloroplasts (Figure 19).⁴⁹ Here is a visible ordered array of particles, each about 200 A in diameter. Whether this structure can be reconstituted from the separated particles remains yet to be demonstrated. The relationship between the energy converting apparatus which the plants use to transform light energy and the energy converting apparatus which both plants and animals use for converting chemical energy is clearly shown in Figure 20 in which are shown both the chloroplasts and the mitochondria in a single plant cell. That the two structures are functionally related, as well as structurally related, seems clear.⁵⁰ Both involve very similar electron transport systems, such as the cytochromes, flavins and quinones as well as their associated proteins. More recently still another molecule in this electron transport chain has been demonstrated in Clostridium bacteria by Carnahan and his associates⁵¹ which seems to be very clearly related, if not identical, to the photopyridine nucleotide reductase which has been isolated from chloroplasts by San Pietro some years ago.⁵² This latter molecule was, according to San Pietro, the one responsible for the transfer of the initially photoexcited electron to pyridine nucleotide, and its demonstration in nonphotosynthetic organisms associated with hydrogen evolution and absorption is just another link in the chain recognizing the very close structural, functional and evolutionary relation between the nonphoto-



ZN-3218

Figure 19. Electron micrograph of "quantasomes"⁵³ from spinach chloroplasts.



Tobacco chloroplasts showing quantasomes in section
Weier, 1962

ZN-3216

Figure 20. Electron micrograph of Elodea chloroplasts,
showing mitochondria (Buvat).

synthetic and the photosynthetic organisms, but on the molecular level. A laboratory demonstration of the coupling of these two molecular systems (hydrogen and pyridine nucleotide reactions) such as exists naturally in some organisms (*Scenedesmus*)⁵⁴ has been published recently by Arnon and co-workers.⁵⁵

Thus we have in our molecular evolution very nearly reached the morphological and anatomical level with which evolutionary studies have long been concerned. It is not difficult to see that the molecular selection processes which we have called upon to develop both the energy transfer and information transfer systems on the molecular level are completely analogous to the selection systems that have been used on the much higher level of structure, and, more recently of biochemical function to demonstrate the nature of the evolutionary process under the pressure of natural selection.

The Cell Membrane

We cannot very well terminate the discussion of chemical and biological evolution without saying a few words relating the earlier processes to the development of the cellular structure itself. The principal requirement would seem to be some mechanism for the appearance of a cellular membrane to encase all the biological apparatus which we have discussed, and much more besides. For this we must call upon the same kinds of spontaneous self-ordering molecular systems that we have used for the energy and information transferring processes earlier.

However, the development of our knowledge of such membrane systems, both in physical-chemical terms as well as in biological terms, is much more rudimentary than we would like to have it.

It is, nevertheless, already possible to demonstrate the same kind of ordering processes that have occurred for the other two functions. The molecules involved here, however, are not water soluble materials but rather water insoluble materials, or molecules, which have only one segment water soluble, the other segment being hydrophobic and more likely to interact with a similar hydrophobic fragment than with water. This type of structural feature is typical of the biologically widespread lipids which we now know to be important in the structure of biological membranes.

It has long been known that such bifunctional molecules form membranous layers spontaneously at the water-air interface -- for example, fatty acids, soaps, and the like. That such materials may form double layer membranes between water and a lipid layer has also been established. I would like to introduce here an example of this spontaneous membrane, or double membrane, formation, a case with which I happen to be personally interested, namely, the case of chlorophyll itself. Here the hydrophilic porphyrin head is attached to a hydrophobic, or lipophilic, phytol tail, and the two together have the essential element of structure which we mentioned earlier. In fact, if they are spread out either at a water-air interface or a water-oil interface they spontaneously take up an ordered array which might be thought of as a two-dimensional crystal

lattice in the same sense that the protein or nucleic acid helix might be called a one-dimensional crystal. This was demonstrated by the change in absorption spectrum shown in Figure 21.⁵⁶ The molecule in a solvent has a noticeably different spectrum from the molecule formed in a layer at a water-air interface or a water-oil interface. It is interesting to note that the spectrum of these chlorophyll layers at either a water-air or water-oil interface is very nearly the same as the spectrum of chlorophyll in the quantasomes and lamellae shown in Figures 19 and 20, suggesting that here the chlorophyll is similarly arrayed.

Still more recently a much more complex membrane structure has been reconstituted from lipids of biological origin and shown not only to have a 60 Å double layered structure but to have electric and selective functionality as well.⁵⁷ I think that work of this sort will eventually demonstrate unequivocally that the membrane structure results from the characteristics of the molecules of which the membrane is constituted.

We must leave at this point our discussion of chemical and biological evolution on the surface of the earth, having arrived at the enclosing of the energy transforming and information communicating apparatus within a cell wall. We have, it would appear, generated the essential elements for the development of multicellular organisms as well, and the sequence of events beginning not much further beyond this is actually recorded in the fossil record.

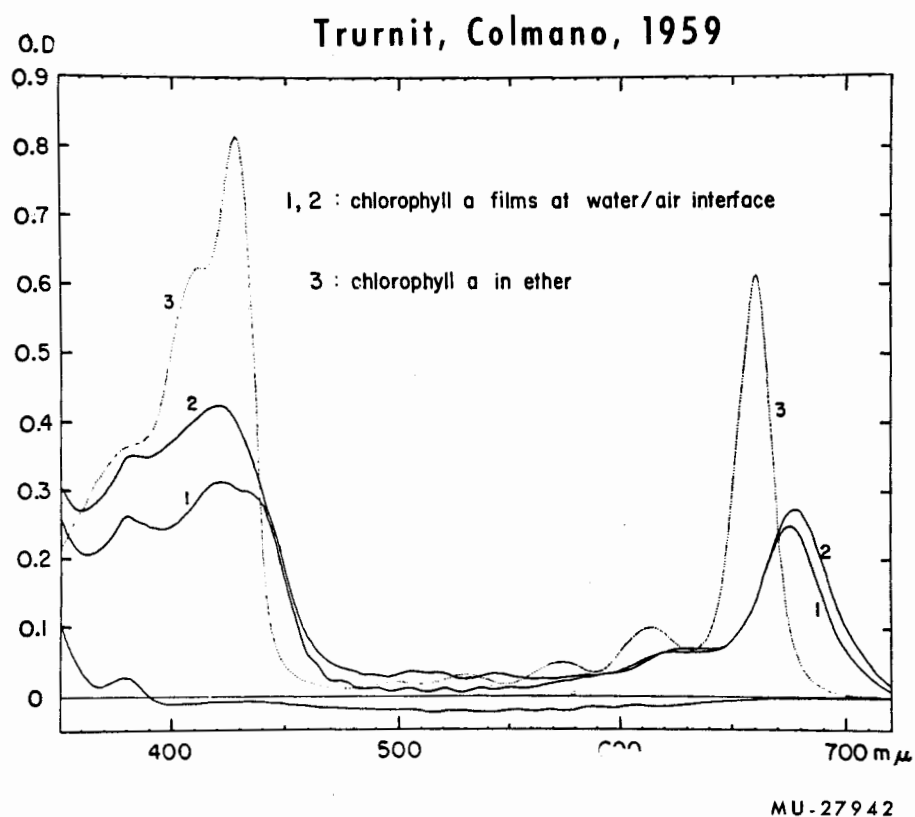


Figure 21. Film spectra of chlorophyll at water-air interface, and solution spectrum.

EXTRATERRESTRIAL LIFE

It appears to me that the information we now have available regarding the nature of molecular evolution which leads up to something which is unequivocally acceptable to all of us as a living organism is such as to impress one with the notion that such a sequence, at least in its earlier stages, results from the concatenation of molecules and energy sources, temperature and environment with its variation, which the primitive earth provided, and it is not a unique accident. If this be the case, we can surmise that given a corresponding set of molecules, temperature and environment anywhere else in the universe, a similar sequence of events might have been expected to occur.⁵⁸ This does not imply that the multicellular end-products that we know today would be identical elsewhere, since the evolutionary process on the surface of the earth is far from having tried all the possible multicellular combinations imaginable. The time has simply not been available for this at the rate it can be done. This is not true for the simple atomic and molecular combinations of the earlier phases, the exploration of which took place at a much higher rate. However, the general pattern of transformation in the early phases would be similar, and in the later phases analogous, to those taking place on the earth, and we have only to answer the question: Are there similar environments elsewhere?

Life Elsewhere in the Solar System

There are two kinds of direct information that we have today about such possibilities in our own solar system. These come to us in the form of electromagnetic radiations, that is, light, both visible, infrared and possibly radio waves, and in the form of the meteorites which we presume have their origin in the asteroid belt between Mars and Jupiter.

The information that is available to us from our direct observations with visible and infrared light seems to suggest quite unequivocally that the Moon, having no atmosphere, is not likely to have on it living organisms of the type we know. This is not to say that the Moon has not acted as a cold storage repository of both molecules and fragments which may have been biological, which it has captured in its long sweep through space accompanying the earth.^{59, 60} Such materials captured by the earth itself would have been long since metamorphosed by the life on it, but may very well be in their primitive condition on the surface of the Moon.

Our next nearest planetary neighbors, however, have somewhat better prospects. Venus in the smaller orbit near the sun is definitely warmer, but it does have an atmosphere and is very nearly the same size as the earth. Its atmosphere seems to be occupied, at least at its higher level, by a cloud impenetrable to visible light. We, therefore, cannot see the actual solid surface of the planet. I shall not try to review here the evidence for the nature of the Cytherean atmosphere. A perusal of various reviews⁶¹ on the subject leaves the impression that we do not really know what the quality of that atmosphere is in an unequivocal fashion and we are thus not severely limited in our conclusions.

The optical data that are available to us about the surface of Mars are somewhat more extensive. Here it has been long since recognized that there is a seasonal variation in the visible color of various parts of the surface of the planet. There is a polar white cap which advances and recedes with the season, and with it there are changes at lower latitudes involving advance and recession of a dark area approximately bordering the polar white cap and a light area beyond it. The dark area is often called green and the light area red, although this is more a subjective phenomena than a spectroscopic one.

Recently the astronomer Sinton has examined the light and dark areas with the infrared spectrometer on the 200-inch telescope, and has seen a larger absorption in the 3.5μ region in the dark area of the planet than in the light area.⁶² This he has interpreted to mean that the dark area does indeed contain C-H linkages, since the 3.5μ region i.e., near 3000 cm^{-1} , corresponds approximately to C-H absorption. If this is indeed true and if the intensity of these C-H components of the infrared absorption (reflection) do indeed vary with the seasons as do the visible changes, then Sinton's observations might very well be the best evidence we have for the existence of organic life as we know it on the surface of Mars. Salisbury⁶³ has even gone so far as to suggest its most probable nature to be a broad leafed plant. However, we are very limited in our ability to get such information from the earth's surface. The resolving power of the telescopes with respect to the geography of Mars is limited when the light has to go through an infrared spectrometer as well.

The identification of the IR bands with C-H frequencies leaves much to be desired, and the identification of the polar white cap as a snow cap has also been recently called into question. It has been suggested that the white cap is not frozen water at all but may very well be frozen N_2O_4 instead.⁶⁴ Casting even more uncertainty is the fact that some of the 3.5 μ absorption seems to correspond fairly closely with one of the NO_2 absorptions, but there is not enough of it.⁶⁵ Further than this, if there were a large amount of NO in the atmosphere of Mars with a small amounts of NO_2 , the blue-green (or dark) color might very well be due to the condensation of small amounts of N_2O_3 whose infrared spectrum is not yet precisely known. Beyond this, we have observed that a variety of inorganic carbonates give reflections in this same 3.5 μ region.⁶⁶ We are thus left with a high degree of uncertainty about the possible existence of carbon-based life on Mars.

However, we need not remain in this ignorance for very long. Many of us will undoubtedly have unequivocal answers to the questions nearest celestial we have raised about all three of our neighbors -- Mars, Venus and the Moon -- certainly within the next decade and possibly much sooner, in view of what has happened in the last year and particularly in the last month. We will certainly have orbiting telescopes which will not be hampered by the content and fluctuation of the earth's atmosphere, and we will thus be able to have a very close look at the optical properties, particularly of Mars, in regions which are today inaccessible to us.

We can also expect very soon to know something of the possible existence of organic material captured on the surface of the Moon, and of its nature. We will probably not have to wait for a man to land on the surface of the Moon to know the answer to this question, since it can be instrumented; it is being instrumented in our country and very likely elsewhere as well. Various types of detecting devices for organic matter and its character will be landed on the surface of the Moon, and will telemeter their findings back to us. Shortly after that we will undoubtedly have men either bringing us back pieces of the Moon or at least telling us of what it is made. A similar sequence of observations will take place with respect to Venus and Mars. However, the time scale will presumably be somewhat longer.

Meteorite Observations

In the meantime, we have another source of information about the construction of our neighbors in the solar system. If we accept the current apparent notion that the origin of the meteorites lies somewhere in our solar system (presumably in the asteroid belt), then a chemical examination of their constitution provides us with some information concerning what such bodies must be constructed of. Aside from their inorganic constituents, which are chemically not greatly different from terrestrial matter (although mineralogically and physically they are), a certain number of such meteorites contain organic matter. This has been known for over one hundred years. However, it is only in recent years that the examination of that organic material has been possible on the

micro scale and with precision and detail that has allowed new conclusions to be drawn as to their origin.

Some years ago we examined the organic constituents of one recently fallen meteorite (Murray, 1950), and came to the conclusion that it not only contained hydrocarbons (at least up to C_{12}), which were purely incidental to our search, but also ultraviolet-absorbing material which resembled heterocyclic bases going into the construction of nucleic acids.⁶⁷ These we interpreted to be representing some of the organic compounds of the primitive solar system upon which chemical evolution operated.

More recently a more detailed examination of the nature of the hydrocarbons in meteorites has been made in the mass spectrometer.⁶⁸ These seem to have an alternation in hydrocarbon size as well as a dominance of the C_{21} fragments which suggested their origin in lipids and steroids. If indeed these materials come in with the meteorites from extraterrestrial sources and do not have their origin on the earth, that would be very good evidence for the existence of primitive organisms elsewhere.

A further, more spectacular conclusion has been drawn from a microscopic examination of a number of meteorites, particularly Orgueil and Mokoia.^{69, 70} Particles of various specific and apparently nonrandom shapes have been claimed as being the fossil remains of extraterrestrial microorganisms. This result has been disputed and the results variously interpreted. We have had a look at some of the ground

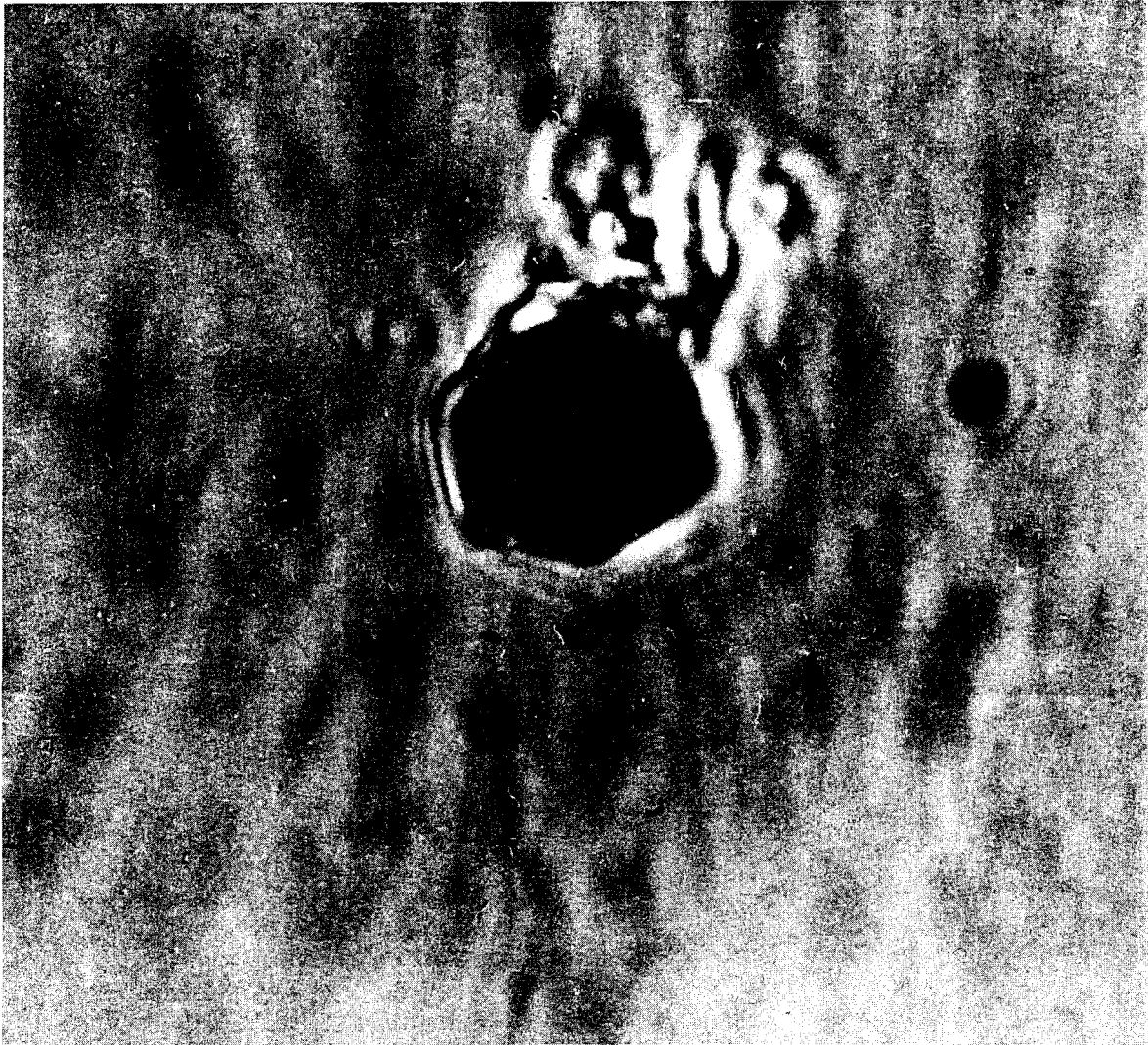
up bits of Orgueil and have seen many more or less regular structures, one of which is shown in Figure 22. I feel that we must reserve judgment as to the nature of these particles⁷¹ as well as to their origin.⁷²

Perhaps in the next decade we will not have to depend upon these random and accidental messengers from outer space but will be able to go and collect samples, if not at will at least with some effort, and thus have a more likely chance to arrive at an unequivocal answer to this important question.

Life in Other Galactic Systems

On the scale of the entire universe we can explore the possibility of the existence of life only statistically. Accepting the current most popular theories of the origin of the stars and the planets around them in terms of a gravitationally condensing cloud of molecules (H_2 , CH_4 , H_2O , NH_3) and dust (the heavier elements in various combinations), one can make the statistical assertion that planetary systems are widespread throughout the universe. One can even go beyond this and assert that there will be a finite probability of many of these extraterrestrial systems containing earth-like planets in those essential aspects for the evolution of life, that is, temperature, size, and molecular environment.⁷³

Thus we are led to the conclusion that there must exist elsewhere in the universe not one but many terrestrial type planets upon which, we therefore conclude, will have evolved living systems of a kind that we would recognize as such. Given the time scale of 5 to 10 billion years,



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Figure 22. Electron micrograph of ground up particles from Orgueil meteorite.

it is clear that some of these living communities may have existed much longer than the one on the earth, and, therefore, one might expect that multicellular organisms having had more time may have progressed far beyond the systems that we know here. Of course, there will be many which have not existed as long, as well, but it is the former which intrigues our imagination more profoundly.

The kind of intelligence we can recognize as man has existed on the surface of the earth for ^a very short period in these terms, and we therefore might expect that in terms of the ability to communicate, some of these other planetary systems may be inhabited by organisms far more skillful and knowledgeable than we. This kind of reasoning has already led to an attempt to listen with our own newly acquired radiotelescopes for messages from such organisms.^{74 11} This has, as yet, been fruitless. However, a bit of careful and controlled imagination as to how we might achieve such contact has led one of our radioastronomers⁷⁵ to invent a possible message which might have arrived from outside the solar system, and I give it to you for your own deciphering.

An Example of a Message That Might be Received
from Another Civilization in Space

11110000010100100000110010000000100000010100
100000110010110011110000011000001101000000
001000000100000100000100010101000001000000000
0000000000010001000000000001011000000000000
000000001000111011010110101000000000000000
0000100100000111010101010000000000101010101
000000000011101010101110101100000001000000
000000000000100000000000001000100111111000
0011101000000101100000011100000000100000000
10000000001000000001111100000001011000101110
1000000001100101111101011111000010011111001
0000000000001111100000001011000011111110000
1000000110000001100000100000110000000011000101
00100001111100101111

Frank Drake
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Green Bank, West Virginia

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